

In re Application of:

Alan Clarke Peterson

Application No.: Not Yet Assigned

US Submission Date: December 30, 2005

Based on Intl Appl: PCT/CA2004/000998

IA Filing Date: July 8, 2004

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B. In the Claims

Please amend claims 4 to 6, 9 to 13, 18 to 19, and 22 to 24 without prejudice.

Upon entry of the present amendment, the claims will stand as follows in the present application:

1. (original) A preparation of non-inbred mouse embryonic stem (ES) cells that comprise alleles derived from at least three different inbred mouse strains, wherein the ES cells have good developmental potential and successfully compete with pre-existing inner cell mass cells, and their derivatives, when injected into a normal blastocyst.
2. (original) The non-inbred ES cell preparation according to claim 1, wherein the ES cells additionally comprise a transgene docking site.
3. (original) A preparation of non-inbred mouse embryonic stem (ES) cells that comprise alleles derived from at least two different inbred mouse strains and a transgene docking site, wherein the ES cells have good developmental potential and successfully compete with pre-existing inner cell mass cells, and their derivatives, when injected into a normal blastocyst.
4. (currently amended) The non-inbred ES cell preparation according to claim 2 or 3, wherein the transgene docking site is a deletion mutant of a hypoxanthine phosphoribosyltransferase (HPTR) gene.
5. (currently amended) The non-inbred ES cell preparation according to claim 2 or 3, wherein the transgene docking site comprises a *loxP* site.

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6. (currently amended) The non-inbred ES cell preparation according to

~~claim 1~~~~any one of claims 1—5~~, wherein chimeras derived from the ES cells exhibit greater than 50% ES cell contribution.

7. (original) The non-inbred ES cell preparation according to claim 6, wherein chimeras derived from the ES cells exhibit greater than 90% ES cell contribution.

8. (original) The non-inbred ES cell preparation according to claim 7, wherein chimeras derived from the ES cells exhibit about 100% ES cell contribution.

9. (currently amended) A method for producing an ES cell-derived mouse comprising the steps of:

(a) introducing a non-inbred mouse ES cell preparation according to ~~claim 1~~~~any one of claims 1—8~~ into a normal mouse blastocysts or a tetraploid mouse blastocysts or aggregating a non-inbred mouse ES cell preparation according to ~~claim 1~~~~any one of claims 1—8~~ with one or more pre-implantation embryos under conditions that result in production of at least one embryo;

(b) transferring the resulting embryo(s) into an appropriate foster mother; and

(c) maintaining the foster mother under conditions that result in development of live offspring.

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10. (currently amended) A method for producing an ES cell-derived, transgenic mouse comprising the steps of:

- (a) introducing one or more transgenic sequences into non-inbred mouse ES cells of an ES cell preparation according to ~~claim 2 any one of claims 2 or 4~~ 8;
- (b) maintaining the ES cells under conditions that result in homologous recombination at the transgene docking site such that the one or more transgenic sequences are incorporated in the genome of the ES cells;
- (c) introducing the resultant recombinant ES cells into normal blastocysts(s) or tetraploid blastocysts(s) or said recombinant ES cells with one or more pre-implantation embryos, under conditions that result in production of at least one embryo;
- (d) transferring the resulting embryo(s) into an appropriate foster mother; and
- (e) maintaining the foster mother under conditions that result in development of live offspring, wherein the ES cells have good developmental potential.

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11. (currently amended) A method for producing an ES cell-derived, gene targeted mouse comprising the steps of:

- (a) performing a genetic alteration or mutation of one or more genes or parts of genes in non-inbred mouse ES cells of an ES cell preparation according to claim 1~~any one of claims 1-8~~;
- (b) maintaining the ES cells under conditions that result in homologous recombination such that the knock-out is incorporated in the genome of the ES cells;
- (c) introducing the resultant recombinant ES cells into normal blastocyst(s) or tetraploid blastocysts(s) or said recombinant ES cells with one or more pre-implantation embryos, under conditions that result in production of at least one embryo;
- (d) transferring the resulting embryo(s) into an appropriate foster mother; and
- (e) maintaining the foster mother under conditions that result in development of live offspring, wherein the ES cells have good developmental potential.

12. (currently amended) The method according to claim 9~~any one of claims 9, 10 or 11~~, wherein the appropriate foster mother is, a pseudopregnant female mouse.

13. (currently amended) An ES cell-derived mouse that is prepared according to the method of claim 9~~any one of claims 9-12~~.

14. (original) The mouse according to claim 13, which is a transgene bearing mouse.

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15. (original) The mouse according to claim 13, which is a genetically altered or mutated mouse.

16. (original) A method for preparing mouse embryonic stem cells having good developmental potential that comprises the steps of:

- (a) mating a female mouse of a first inbred mouse strain with a male mouse of a second inbred mouse strain, wherein the first and the second mouse strains are different;
- (b) performing multiple generations of breeding including a combination of at least one cross and at least one backcross from offspring obtained from the mating between the female mouse and the male mouse in step (a);
- (c) recovering blastocysts from a mouse obtained following the multiple generations of breeding performed in step (b); and
- (d) deriving embryonic stem cells from the inner cell masses of said blastocysts.

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17. (original) A method for preparing mouse embryonic stem cells having good developmental potential that comprised the steps of:

- (a) mating a female mouse of a first inbred mouse strain with a male mouse of a second inbred mouse strain, wherein the first and the second mouse strains are different;
- (b) mating an offspring of the mating of step (a) or an offspring of a subsequent generation with a mouse of a third inbred mouse strain;
- (c) performing multiple generations of breeding including a combination of at least one cross and at least one backcross from offspring obtained from the mating of step (b);
- (d) recovering blastocysts from a mouse obtained following the multiple generations of breeding performed in step (c) and
- (e) deriving embryonic stem cells from the inner cell masses of said blastocysts.

18. (currently amended) The method according to claim 16 or 17, wherein the multiple generations of breeding comprises a combination of 5 or 6 crosses and backcrosses.

19. (currently amended) The method according to ~~claim 16 and one of claims 16–18~~, wherein at least one of the inbred mouse strains contains a transgene docking site.

20. (original) The method according to claim 19, wherein the transgene docking site is a deletion mutant of a hypoxanthine phosphoribosyltransferase (HPTR) gene.

21. (original) The method according to claim 19, wherein the transgene docking site comprises a *loxP* site.

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22. (currently amended) A non-inbred embryonic stem (ES) cell preparation obtained by the method of claim 16~~any one of claims 16-21~~.

23. (currently amended) Use of the ES cell preparation according to claim 1~~any one of claims 1-8 or 22~~ for producing an ES cell derived mouse.

24. (currently amended) Use of the ES cell preparation according to claim 1~~any one of claims 1-8 or 22~~ for producing an ES cell derived genetically modified mouse.

25. (original) The use according to claim 24, wherein said genetically modified mouse is a transgenic mouse.

26. (original) The use according to claim 24, wherein said genetically modified mouse comprises a genetic alteration or mutation.